

Application No.: 09/747,004  
Attorney Docket No.: 3366.1

## REMARKS

### *Status of the claims*

Claims 1-27 remain pending in the application. Claims 15 and 16 have been amended to recite to correct the dependencies of the Claims. Support for the amendment can be found, for example, on pages 33-34 of the Specifications. Claims 26 and 27 have been added, support for these amendments can be found, for example, in the original claims.

### *Claims Rejections under 35 U.S.C 112, second paragraph should be withdrawn*

Claims 15 and 16 have been rejected under 35 U.S.C 112 by the Examiner for allegedly being indefinite for insufficient basis of the limitation "the pool of target nucleic acid in Claim 15 and "pool of target nucleic acids" in Claim 16. Claims 15 and 16 have been amended to recite "the pool of mRNAs". Furthermore, Claims 15 and 16 have been amended to correct the dependencies of the Claims. New claims 25-27 have been added. It is thus submitted that the claims meet the requirement of 35 U.S.C. 112, second paragraph and withdrawal of the present rejection is respectfully requested.

### *Claims Rejections under 35 U.S.C. 102 should be withdrawn*

Claims 1-6, 12, 15-18 have been rejected by the Examiner under 35 U.S.C. 102(b) as being anticipated by Irvine et al. (U.S. Patent 5,736,316). Applicants respectfully disagree with the Examiner.

The invention relates to the detection of a plurality of different nucleic acid targets by hybridization of the targets with two oligonucleotides probes. Specifically, independent Claim 1 provides a method for detecting at least 50 targets using a at least 50

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mediator nucleic acids" comprising a first subsequence that is complementary to one of the targets and a second subsequence that is complementary with one of the cipher probes and at least 50 different cipher probes immobilized on a microarray.

Irvine et al. discuss a sandwich hybridization assay for detecting a single analyte (i.e. HBV) using multiple oligonucleotides: a set of amplifier probe oligonucleotides (mediator nucleic acids), a set of capture probe oligonucleotides, an oligonucleotide bound to the solid phase (cipher probe), a nucleic acid multimer and a labeled oligonucleotide. The capture probe has a segment having a nucleotide sequence complementary to a segment on the analyte and a second segment having a nucleotide sequence complementary to an oligonucleotide bound to the a solid phase (Col 2, lines 33-39). The amplifier probe has a segment having a nucleotide sequence complementary to a segment on the analyte and a second segment having a nucleotide sequence complementary to an oligonucleotide unit of the nucleic acid multimer. The bound product is then contacted with a nucleic acid multimer comprising a region complementary to a labeled oligonucleotide and the bound complex is detected by hybridization with a labeled oligonucleotide. Irvine et al. use a set of amplifier and capture probes binding different sequences of a same analyte (see Col 5, lines 12-13). A number of different amplifier and capture probes is used to increase the sensitivity of the assay (i.e. the detection of the analyte). Irvine et al. does not teach or disclose the detection of at least 50 nucleic acids by hybridization with at least 50 mediator nucleic acids and at least 50 different cipher probes.

Since Irvine et al. do not disclose every element of the claim 1, Applicants respectfully request that the rejection of Claims 1-6, 12, and 15-18 under 35 U.S.C 102(b) be withdrawn.

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Claims 1-18 and 21-24 have been rejected by the Examiner under 35 U.S.C. 102(e) as being anticipated by Felder et al. (U.S. Patent No. 6,232,006 B1). Applicants respectfully disagree with the Examiner.

Felder et al. discuss a method of detecting nucleic acid targets in high throughput fashion using 96 well microplates, each well having 36 different tests performed in it by using an array of about 36 anchors (cipher probes) and linkers (mediator nucleic acids).

However, in Felder et al., the same anchors are used for all screening assays (i.e. in each well; see Col. 2, line 40, Col.3 lines 27-32 and Figure 2) and each well is therefore "specific for as many as 36 different targets" (Col 2, lines 42-43). The assay described by Felder et al. enable to assay as many as 96 samples (for example 96 cell lines, tissues...) at the same time for the presence of as many as 36 different target nucleic acids.

In contrast, the methods of Claim 1 use at least 50 different cipher probes and mediators for the detection of "at least 50 nucleic acid targets". Therefore, the methods discussed by Felder et al. do not meet the "at least 50 nucleic acid targets" limitation. Since Felder et al. do not disclose every element of Claim 1, Applicants respectfully request that the rejection of Claims 1-18 and 21-24 under 35 U.S.C 102(e) be withdrawn.

***Claims Rejections under 35 U.S.C. 103 should be withdrawn***

Claims 19 and 20 have been rejected by the Examiner 35 U.S.C. 103(a) as being unpatentable over Felder et al. (U.S. Patent No. 6,232,006 B1) in view of Southern et al. (U.S. Patent No. 6,150,095). Applicants respectfully disagree with the Examiner.

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As discussed above, the primary reference Felder et al., fails to teach all the limitations of Claim 1. Southern et al. is cited as providing a technique of synthesizing probes on a substrate in the 5'-3' direction or the 3'-5' direction and does not remedy to the deficiencies of the primary reference. Therefore, Applicants respectfully request that rejection of Claims 19 and 20 under 35 U.S.C. 103(a) be withdrawn.

Claims 19 and 20 have been rejected by the Examiner 35 U.S.C. 103(a) as being unpatentable over Irvine et al. (U.S. Patent No. 5,736,316) in view of Southern et al. (U.S. Patent No. 6,150,095). Applicants respectfully disagree with the Examiner.

As discussed above, the primary reference Irvine et al. fails to teach all the limitations of Claim 1. Southern et al. is cited as providing a technique of synthesizing probes on a substrate in the 5'-3' direction or the 3'-5' direction and does not remedy to the deficiencies of the primary reference. Therefore, Applicants respectfully request that rejection of Claims 19 and 20 under 35 U.S.C. 103 be withdrawn.

### CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

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If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,

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